THE CLEMMENSEN REDUCTION *CUM* REARRANGEMENT OF *ALPHA*-AMINOKETONES

BY

SEEMON HAYDEN PINES

B.S., Lehigh University, 1948
M.S., University of Illinois, 1949

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1951

URBANA, ILLINOIS

1951

THE CLEMMENSEN REDUCTION *CUM* REARRANGEMENT OF *ALPHA*-AMINOKETONES

BY

SEEMON HAYDEN PINES

B.S., Lehigh University, 1948
M.S., University of Illinois, 1949

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1951

URBANA, ILLINOIS

1951

ACKNOWLEDGEMENT

The author desires to express his sincere thanks to Dr. Nelson J. Leonard for suggesting this work, for his advice and encouragement, and for his constructive criticism throughout the past two years.

The author is also grateful to the University of Illinois for fellowships during the period September, 1949, to June, 1951.

R. UNIV.
BIBLIOTHEEK
LEIDEN

THE CLEMMENSEN REDUCTION *CUM* REARRANGEMENT OF *ALPHA*-AMINOKETONES

Introduction

The rearrangement of six- and seven-membered cyclic α-aminoketones under the conditions of the Clemmensen reduction has been shown to be a general rule.[1] This generality extends to both mono- and bicyclic systems in which the nitrogen atom is fully substituted. It has also been demonstrated that these aminoketones undergo rearrangement whether the *alpha*-carbon atom is unsubstituted, monoalkyl-, or dialkyl-substituted.

As notable exceptions to this reaction, Clemo and his coworkers[2] have reported that neither 3-ketoquinolizidine nor 3-ketoquinuclidine rearranges upon Clemmensen reduction, whereas both of these possess the structure considered requisite for rearrangement. In the case of the former, this nonconformity appeared striking, since the isomeric 1-ketoquinolizidine has been shown to rearrange to 1-azabicyclo-[5.3.0.]decane under Clemmensen reduction.[3]

This investigation was carried out in an attempt to determine further the scope of the reduction *cum* rearrangement of α-aminoketones. Both 3-ketoquinolizidine and 3-ketoquinuclidine were synthesized and subjected to the Clemmensen reduction.

The influence of substitution on the nitrogen atom upon the rearrangement was also studied. Accordingly, 2-ethyl-3-piperidone was synthesized and its Clemmensen reduction product studied.

Discussion Of Results

The synthesis of 3-ketoquinolizidine has been accomplished

by the method of Clemo, Morgan, and Raper.[2] It has been established that the product of Clemmensen reduction of this aminoketone is 3-methyloctahydropyrrocoline, the two racemates of which have been obtained for the first time. Chromatographic adsorption on a column of alumina served as an effective method of separation of the racemates. These findings are contradictory to the earlier work of Clemo, Morgan, and Raper,[2] who reported quinolizidine as the Clemmensen reduction product.

The results reported by Clemo and Metcalfe[2] describing the Clemmensen reduction product of 3-ketoquinuclidine as quinuclidine have been verified and extended. Clemmensen reduction of the same aminoketone at 17-19° C. also yields quinuclidine.

A cyclic secondary α-aminoketone has been prepared for the first time by Dieckmann cyclization of the requisite diester, followed by hydrolysis and decarboxylation. It has been shown that Clemmensen reduction of this compound, 2-ethyl-3-piperidone, followed by the usual procedure of isolation from alkaline medium results in the formation of 2-*n*-propylpyrroline, and that this same pyrroline, once isolated, can be reduced readily under Clemmensen conditions to 2-*n*-propylpyrrolidine. These results showed conclusively that the complete reduction (with rearrangement) of cyclic secondary α-aminoketones must be a two-step process. The direct conversion of 2-ethyl-3-piperidone to 2-*n*-propylpyrrolidine could not be accomplished by usual variations in the Clemmensen conditions.

Some observations concerning a previously postulated mechanism[4] for reduction-rearrangement have been presented.

BIBLIOGRAPHY

1. Leonard *et al*, J. Am. Chem. Soc., 71, 3089, 3094, 3098, 3100 (1949); 72, 3632 (1950).

2. Clemo *et al*, J. Chem. Soc., 1743 (1935); 1989 (1937).

3. Clemo *et al, ibid.*, 1429 (1936) ; Prelog and Seiworth, Ber., 72, 1638 (1939).

4. Clemo *et al*, J. Chem. Soc., 2095 (1940) ; Chem. and Ind., 856 (1949).

VITA

The author was born in Portland, Maine, on January 3, 1926. He attended public schools in Portland, New York City, and Pottsville, Pennsylvania. He was graduated from Pottsville High School in June, 1942. He entered Lehigh University in September of the same year, receiving the degree of Bachelor of Science in Chemical Engineering in June, 1948. Two of the interim years, 1944 to 1946, were spent in the United States Navy. He entered the Graduate College of the University of Illinois in the fall of 1948, and was granted the degree of Master of Science the following Spring. While at Urbana, he held second- and third-year University Fellowships.

Digitized by the Internet Archive
in 2026

https://archive.org/details/IA41549816_0189